phenomena, one a function of the condition of life of the nerve and the other a physical phenomenon dominated by the salt content of the nerve, and capable of continuation long after its death.

* * * * *

6. If a number of threads are twisted together to form a rope and the rope laid upon two non-polarisable electrodes of the usual type, no current is found between the electrodes if the thread rope is previously uniformly wetted with a saline solution or with tap water. If on such an uniformly wetted rope a drop of saline solution of a different concentration is placed at a point closer to one electrode than another a current is found in the circuit, and a source of E.M.F. quite comparable in value to the maximal value of the demarcation source of a nerve. A drop of the same solution placed upon a corresponding point of the rope nearer to the other electrode may reduce, bring to zero, or reverse this difference of potential.

This phenomenon is presumably due to the upsetting of the balance between the osmotic processes taking place in the two non-polarisable and "similar" electrodes.

* * * * *

7. The close association of the value of the demarcation current with the salt content of the nerve suggests a similarity between the experimental phenomena observed in the thread and in the nerve, and the causation of the demarcation current of nerve as due to a balance between two unequal osmotic processes, one at the cross section and one at the longitudinal surface.

* * * * *

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"The Demarcation Current of Mammalian Nerve. (Preliminary Communication.) II. The Source of the Demarcation Current considered as a Concentration Cell." By J. S. MACDONALD, B.A., L.R.C.P.E., University College, Liverpool, Research Scholar of the British Medical Association. Communicated by Professor SHERRINGTON, F.R.S. Received September 25, 1900.

The changes produced by the action of tap water upon the nerve have, in the interval, been more closely studied. Excluding alterations of E.M.F., they are as follows:—

An increase of
- (a) weight.
- (b) length.
- (c) rigidity.
- (d) elasticity.

A diminution of
- (a) compressibility.
- (b) conductivity.

Thus a piece of sciatic nerve (cat) examined before and after an mersion of 20 minutes in tap water :—

	Before.	After.
Weight in grammes...............	0·237	0·317
Length in centimetres............	4·8	5·4
Resistance in ohms	14,200	18,400

The general condition is known, and has been previously described as "water rigor"; a similar change produced by the action of water upon muscle has been found (see Fletcher*) to be unattended by the chemical changes accompanying other forms of rigor.

With the exception of the change in conductivity, all the changes are rapidly developed, reaching their maxima within an hour after immersion in water; they may remain for days in an approximately maximal condition, but are at any time abolished by a short immersion in 0·9 per cent. "saline." The change in conductivity is a much more gradual one, as is well shown by the details of an experiment. In the following experiment the appearances of rigor were fully developed within the first hour, the available E.M.F. had also risen to its maximum (0·027 volt as contrasted with the initial value 0·018 volt), whereas the nerve still retained 70 per cent. of its original conductivity.

Experiment.—Sciatic Nerve of Dog.

Length of piece used, 5 cm.

The initial resistance having been measured, the nerve was placed in tap water (1 litre) from which it was removed every twenty-five minutes for re-examination.

* 'Journal of Physiology,' vol. 23, i, ii, 85.

	Resistance.	
	In ohms.	In terms of the original as unity.
Nerve at first	15,900	1·00
$\frac{1}{2}$ hour	20,400	1·28
1 ,, ...	23,100	1·45
$1\frac{1}{2}$,, ...	28,800	1·81
2 ,, ...	39,800	2·50
$2\frac{1}{2}$,, ...	51,100	3·21
3 ,, ...	54,900	3·45
$3\frac{1}{2}$,, ...	61,000	3·84
4 ,, ...	88,700	5·58
* *	*	*
24 hours	307,500	19·34

The condition of rigor is most completely produced by the action of water, but in all the characteristics observed differs only in degree from similar conditions produced by dilute saline solutions, *e.g.*, 0·6 gramme per cent. NaCl solution.

In the latter we get the same increased rigidity, weight, length, &c., as also the diminution of conductivity; all of these, however, are found to a smaller measure, and are much less persistent.

Although not provided with the evidence of direct analysis, it seems very reasonable to assume that both the extreme and the lesser variations, as judged by the character of the changes observed, are to be explained by the occurrence of "osmosis" and "diffusion"; and that in the extreme case, the nerve continues to acquire water until a very considerable internal pressure is produced, thereby causing the extreme changes of form and elasticity, whereas the conductivity is gradually diminished through an increasing loss of electrolytes by processes of diffusion.

It is worthy of note that the appearance is quite different in character and degree from the slight rigidity change which ordinarily, in nerves, follows the death of an animal, and that it can be produced by a short immersion in tap water in a nerve removed from the body of a "several days dead" dog, or in a nerve which has lain for days in saline solutions, and therefore is in no way dependent upon the living state of any of the structures of the nerve. Finally, as a minor proof that it is not produced by the precipitation of globulins in the nerve, it is completely and at once abolished by immersion in a saturated solution of magnesium sulphate.

* * * * *

The graduated character of the changes produced and their parallelism with the graduated concentration of the solutions has been carefully followed out; for the sake of brevity, however, data are given

here only from the three experiments which seem to determine the strength of the isotonic solution as showing a minor degree, an absence, and a reversal of the condition.

Experiment A.—Sciatic Nerve of Cat.

The nerve was examined (A) at once, and 1, 2, 3, &c., after successive immersions of ten minutes' duration in a 0·6 gramme per cent. NaCl solution.

	A.	(1.)	(2.)	(3.)	(4.)	(5.)
Ohms	19,200	22,600	21,200	20,900	20,600	20,700
Volts............	0·018	0·023	0·020	0·016	0·013	0·011
Grammes	0·207	0·213	0·221	0·227	0·233	0·236
Centimetres	4·9	5·1	5·1	5·1	5·1	5·1

An error is evidently introduced into the measurement of resistance, if we wish to consider the resistance of a cylinder of the nerve of constant length and cross section, by the increase in volume attending the increase of weight.

Failing an actual determination of the area of the cross section, or one of the volume from which it might be directly obtained by dividing by the length, the value of the weight found in grammes has been treated as volume in cubic centimetres, and used in this way. The error introduced by a neglect of the specific gravity is not, in the case considered, appreciable.

The "specific resistances" for unit length and cross section found in this way from the figures given are—

A.	(1.)	(2.)	(3.)	(4.)	(5.)
165	184	180	182	184	188 ohms.

Experiment B.—Sciatic Nerve of Cat.

The experiment was in every way similar to the last, with the single exception that the solution used was an NaCl solution of 0·75 gramme per cent.

	A.	(1.)	(2.)	(3.)	(4.)	(5.)
Ohms	20,700	20,600	20,200	19,400	18,900	19,200
Volts..........	0·018	0·018	0·018	0·017	0·015	0·014
Grammes	0·210	0·218	0·222	0·228	0·229	0·229
Centimetres	4·6	4·7	4·7	4·7	4·7	4·7
"Specific resistances"	205	203	203	200	196	199

Experiment C.—Sciatic Nerve of Cat.

Similar experiment. Solution used 0·9 gramme per cent. NaCl.

	A.	(1.)	(2.)	(3.)	(4.)	(5.)
Ohms	20,300	18,700	16,700	16,900	17,100	16,100
Volts	0·014	0·014	0·011	0·009	0·009	0·009
Grammes	0·236	0·247	0·257	0·262	0·260	0·260
Centimetres	5	5	5	5	5	5
"Specific resistances"	191	184	171	177	177	167

Taking the three experiments and examining the variations in the specific resistance in each case, it is noticeably least affected in the 0·75 per cent. solution, which therefore, from this point of view, most nearly approaches the "isotonic solution."

Reducing the data from the three experiments to an assumed average value of 200 ohms for the inital resistance, we have

	Initial resistance.	After successive immersions in the solutions.				
		(1.)	(2.)	(3.)	(4.)	(5.)
Experiment with 0·6 per cent.	200	222	218	220	222	228
,, ,, 0·75 ,,	200	198	198	194	190	194
,, ,, 0·9 ,,	200	192	178	184	184	174

or, taking averages from the five determinations made after immersion in the solution,

	Initial.	Final specific resistance.	Total increase.
0·6 per cent.	200	225	+25 ohms
0·75 ,, ...	200	195	−5 ,,
0·9 ,, ...	200	185	−15 ,,

The alteration in weight in the three experiments is apparently anomalous, as there is an increase in each case, and judged from this criterion alone, none of the solutions are isotonic. Considerable care was taken to dry off the superficial moisture, and as far as possible the precautions were the same in each case. There is a difference in

the character of the increase which is confirmed by the results of other experiments, the increase in the hypotonic solution is progressive, in the other two there is an increase to, and a maintenance of, a steady maximal weight. It seems evident that in all three cases there is an imbibition of saline solution at first, apart from any question of the transference of water through a membrane.

The appearances of rigidity were noticeable in the nerve immersed in the 0·6 per cent. solution, though the only index of their occurrence found in the figures given is provided by the increase in length. The occurrence of the appearances is, however, unmistakable in an actual experiment; the difference between a nerve which has been immersed in 0·9 per cent. and one which has been in 0·6 per cent. is quite a marked one.

* * * * *

Markedly graduated as are the changes of weight, length, resistance, and rigidity following the immersion of nerves in solutions of graduated concentration, the changes in the E.M.F. available between cross-section and longitudinal surface are no less so. In so far is this true that it is possible, knowing the initial value of the E.M.F., to predict the value which will be found after immersion of the nerve for a given time in a solution of known concentration at a constant temperature.

The accompanying data are taken from the records of 8 entirely separate experiments. In each, a sciatic nerve (cat), removed immediately after the death of the animal, was cut to a definite length of 5 cm., and placed for 25 minutes in 500 c.c. of an NaCl solution, at a temperature of 17° C.

The E.M.F. found after immersion is given expressed in terms of the initial E.M.F. used as unity, is called the E.M.F. "recovered," and as will be seen is sometimes greater than the initial value.

Solution used.	Proportion of E.M.F. recovered.
(1) Tap water	1·5
(2) 0·6 gramme NaCl per cent.	1·059
(3) 0·75 ,, ,, ,,	0·921
(4) 0·9 ,, ,, ,,	0·786
(5) 1·8 grammes ,, ,,	0·388
(6) 3·0 ,, ,, ,,	0·237
(7) 6·0 ,, ,, ,,	0·107
(8) 9·0 ,, ,, ,,	0·062

If in each case the value of the concentration of the NaCl solution is multiplied by the E.M.F. recovered (expressed in terms of the initial E.M.F.), we get a value which is almost constant for the whole series.

$$
\left.
\begin{array}{l}
(2)\ 0{\cdot}6 \times 1{\cdot}059 = 0{\cdot}6354 \\
(3)\ 0{\cdot}75 \times 0{\cdot}921 = 0{\cdot}69075 \\
(4)\ 0{\cdot}9 \times 0{\cdot}786 = 0{\cdot}7074 \\
(5)\ 1{\cdot}8 \times 0{\cdot}388 = 0{\cdot}6984 \\
(6)\ 3{\cdot}0 \times 0{\cdot}237 = 0{\cdot}7110 \\
(7)\ 6{\cdot}0 \times 0{\cdot}107 = 0{\cdot}6420 \\
(8)\ 9{\cdot}0 \times 0{\cdot}062 = 0{\cdot}5580
\end{array}
\right.
$$

Which relationship can be interpreted to mean that for a considerable range of concentrations the E.M.F. "recovered" varies almost exactly inversely as the concentration, and outside this range the deviation from the law is not great.

The value of the constant, which is practically 0·70, is evidently the concentration of a saline solution in which the E.M.F. should be unaltered by the immersion.

The preservation of a constant temperature throughout the series of experiments is of importance, the variation with temperature being considerable, and complicated. Data are given from a few experiments made to determine the interest of this point.

The data are as before, each from a separate experiment upon a measured length (5 cms.) of the sciatic nerve of a cat; the only difference being in fact that the temperatures of the solutions were varied instead of their concentrations.

Temperature of solution.	Concentration of solution.	E.M.F. "recovered" in terms of the original as unity.
9° C.	·75 per cent. NaCl.	1·01
17	,, ,,	0·92
28	,, ,,	0·62
38	,, ,,	0·62
*	*	*
9° C.	3·0 per cent. NaCl.	0·25
17	,, ,,	0·24
27	,, ,,	0·11
34	,, ,,	0·04
2	,, ,,	0·15

It may seem an obvious and foregone conclusion that the isotonic solution, in which the nerve may lie with the minimal disturbance due to the transference of water and salts, should closely coincide with the solution in which the E.M.F. is retained constant, and also with the probable isotonicity of the solution which in the living body bathed the outer surface of the nerve.

It may indeed be maintained that from the point of view of the established hypothesis the local short circuiting of the demarcation source would be affected by solutions varying in concentration from

the "normal saline" in just such a way as to cause exactly the variations described in the apparent value of the E.M.F., and that the variations would be connected by the simple law found.

If so, an examination of the alterations taking place in the same "normal solution" when its temperature is varied presents an anomaly for explanation. The solution maintained at anything approaching the temperature of the body, in which the E.M.F. would remain constant, is not 0·70 per cent., but 0·45 per cent. NaCl solution.

A more striking anomaly still is obtained when an appeal is made to solutions of electrolytes other than NaCl; an extreme instance is given by the consideration of solutions of NaOH.

The following data are taken from four separate experiments in which 5 cm. pieces of sciatic nerves (cat), removed immediately after death, were placed in each case in 500 c.c. of an NaOH solution at a temperature of 17° C., and left in it for 25 minutes.

Solution.	E.M.F. "recovered."
(1) 0·025 gramme per cent. NaOH.	1·620
(2) 0·050 ,, ,, ,,	0·922
(3) 0·050 ,, ,, ,,	0·800
(4) 0·100 ,, ,, ,,	0·422

Proceeding as before, and multiplying the concentration by the E.M.F., we have

$$
\begin{aligned}
(1)\ 0{\cdot}025 \times 1{\cdot}620 &= 0{\cdot}0405 \\
(2)\ 0{\cdot}050 \times 0{\cdot}922 &= 0\ 0461 \\
(3)\ 0{\cdot}050 \times 0{\cdot}800 &= 0{\cdot}0400 \\
(4)\ 0{\cdot}100 \times 0{\cdot}422 &= 0{\cdot}0422.
\end{aligned}
$$

The concentration law is the same as for NaCl, but the "constant" solution is 0·04 instead of 0·7. Dividing these figures by the molecular weights of NaOH and NaCl respectively, the proportion existing between them is 1 to 12; and this, even allowing for the greater conductivity of NaOH solutions, is evidently a relation of a more complex kind than that found when passing from one concentration to another of a solution of the same electrolyte.

* * * * *

In certain types of experiments, such as those in which the effect of tap water was studied (*vide supra*) upon the nerves of animals in a state of *rigor mortis*, the capacity of the established hypothesis to explain the facts is strained to an absurd degree. The following are brief descriptions of typical experiments concerning which the same statement may safely be made:—

I. *Experiment. Sciatic Nerve of Cat.*

Piece 5 cm. long. Difference of potential taken between the cross section and a point 1 cm. distant.

	Volt.
At once	0·015
After 25′ in 9 per cent. NaCl solution at 17° C.	0·001
Another 25′ ,, ,, ,,	0·001
Another 25′ ,, ,, ,,	0·001
Another 10′ ,, ,, ,,	0·001
After 15′ in tap water at 17° C.	0·011
After another 30′ in tap water at 17° C.	0·022

One hour and 40 minutes in the very "abnormal" saline solution of 9 per cent. NaCl and a subsequent 45 minutes in the very "abnormal" saline solution of tap water, and yet the vigour of the changes is unimpaired—they are displayed to the same abnormal degree by the effects of tap water upon the local circuit, *and the contrasted states of activity and hyperactivity are shown in exactly the same situations.*

II. *Experiments upon Degenerated Nerve.*

In these experiments the preliminary operations for section of the nerves were performed by Professor Sherrington, F.R.S. They are described in the briefest possible manner, but as the nerves were made the subject of systematic and detailed study the full description is withheld, as in case of the other experiments, for an opportunity for more detailed publication.

Experiment α. Vagus of Dog.

Preliminary Operation.—1 cm. of nerve excised at upper limit, and 1 cm. of nerve excised at the lower limit of the nerve in the neck.

Examination nine days afterwards.

Degenerated Nerve.	Intact vagus of other side.
E.M.F. = 0·000 volt.	E.M.F. = 0·006 volt.
Several cross-sections were tried.	
After an immersion of 25′ in tap water—	After an immersion of 25′ in tap water—
E.M.F. = 0·017 volt.	E.M.F. = 0·016 volt.

Experiment β. Sciatic Nerve of Dog.

Preliminary Operation.—1 cm. of nerve excised.

Examination twelve days afterwards.

Degenerated Sciatic.	Intact Sciatic.
E.M.F. = 0·003 volt.	E.M.F. = 0·017 volt.
After immersion in tap water.	After immersion in tap water.
E.M.F. = 0·025 volt.	E.M.F. = 0·026 volt.

* * * * *

It seems highly probable to the author, biased by the simplicity of the "concentration law," that the extreme case studied, namely, the nerve after immersion in tap water, is but an extreme variation of a pre-existing condition—in fact, that the internal structures of the nerve form what is to all intents and purposes a stronger aqueous solution of electrolytes than is found in its superficial parts, just such an arrangement of solutions as the character of the resistance and internal polarisation of nerves has always made probable.

If this is true, all the arguments which can be adduced to explain the E.M.F. obtained from the extreme case can be transferred, when modified, to the normal condition.

In this extreme case there is no need to invoke a difference in the distribution of the dissociation phenomena of life to explain the existence of a source of E.M.F. The source is granted as soon as it is determined that solutions of different concentration, such as are present, are asymmetrically placed in the otherwise symmetrical arrangement of solutions connecting the metallic electrodes.* Failing an absolute knowledge of this asymmetry, there are many reasons which make it highly probable; the anatomical conditions are obviously asymmetrical.

The mathematical considerations determining the value of such a source have been so perfectly elaborated, and consequently simplified, that the data collected from the examination of a supposed instance, even of a complicated case, can be afforded a criticism of great exactness.

With a view to such criticism the research is being continued, and for the present the conditions of a possible reversal are sought.

Throughout the conduct of this research I have been most liberally assisted with information and advice by Professor C. S. Sherrington, F.R.S., and Professor Oliver Lodge, F.R.S., for which I take this opportunity for expressing my gratitude. I have also to thank Mr. B. Davies, Mr. A. Hay, and Mr. W. H. Derriman for their frequently sought opinions, and Mr. W. G. Lloyd for practical assistance in some of the experiments.

* Concentration cells of Nernst, 'Electrochemistry,' Le Blanc.